

Healthy ageing from birth to age 84 years in the Helsinki Birth Cohort Study, Finland: a longitudinal study

Tuija M Mikkola, Hannu Kautiainen, Mikaela B von Bonsdorff, Niko S Wasenius, Minna K Salonen, Markus J Haapanen, Eero Kajantie, Johan G Eriksson



Summary

Background The true prevalence of healthy ageing on a population level is unknown. In this study we aimed to examine the upper limit for the prevalence of healthy ageing, by quantifying the probability of surviving and remaining free of chronic diseases that could impact functioning (ie, healthy survival) across adulthood. We also estimated the prevalence of clinically assessed healthy ageing, and the determinants of healthy survival and healthy ageing.

Methods In this longitudinal study, we assessed men and women born in 1934–44 from the Helsinki Birth Cohort Study (Helsinki, Finland; n=13 140). We obtained information on chronic diseases, deaths, and early-to-midlife variables from national registers, databases, and health records for the period Jan 1, 1971, to Dec 31, 2017 (follow-up 951 088 person-years). We also collated data from clinical visits conducted in 2001–04 and 2017–18. Healthy ageing was defined on the basis of clinical data according to six criteria covering chronic diseases, cognitive function, physical performance, depressive symptoms, pain interference, and social functioning. We analysed the probability of healthy survival across adulthood using the Kaplan-Meier method, and the determinants of healthy survival using Cox regression models. We assessed the association of healthy ageing status in 2017–18 (n=813 with available data) with late-midlife factors collected in 2001–04 using age-adjusted logistic regression.

Findings The probability of healthy survival was 42·8% (95% CI 41·6–44·0) in men and 40·1% (38·9–41·4) in women at age 65 years, and 22·5% (21·5–23·6%) in men and 24·4% (23·3–25·6) in women at age 75 years. Healthy survival was associated with socioeconomic position in childhood (adjusted hazard ratio [aHR], upper-middle class vs manual worker, men: 1·21 [1·11–1·31]; women: 1·15 [95% CI 1·05–1·26]) and years of education (aHR per 1 SD increase, men: 1·12 [1·08–1·16]; women: 1·03 [1·00–1·07]). In men, healthy survival was also associated with lower maternal BMI in late pregnancy (aHR per 1 SD increase 0·93 [0·90–0·96]), and in women, with shorter height at age 7 years (aHR per 1 SD increase 0·95 [0·91–0·99]). Among the 813 individuals with relevant clinical assessment data, 159 (19·6%) met all six criteria for healthy ageing at mean age 76 years (SD 3). In addition to age, we found that nutrition (Alternative Healthy Eating Index, age-adjusted odds ratio [aOR] per 1 point increase 1·03 [1·01–1·05]), former smoker status (vs non-smoker status, aOR 0·68 [0·47–0·98]), and use of lipid-lowering medication (vs not used, aOR 0·60 [0·42–0·87]) in late midlife (mean age 61 years [SD 3]) were associated with healthy ageing.

Interpretation The probability of healthy survival, as the upper limit for healthy ageing, was less than 50% from age 65 years. The probability of healthy survival and healthy ageing was influenced by several factors across the life course. Promotion of healthy ageing needs to take a life course approach.

Funding Signe and Ane Gyllenberg Foundation, Samfundet Folkhälsan, Finska Läkaresällskapet, Medicinska Understödsföreningen Liv och Hälsa, European Commission Seventh Framework Programme, EU Horizon 2020, and the Academy of Finland.

Copyright © 2023 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.

Introduction

Ageing is a primary driver of functional decline and chronic diseases. The definition of healthy ageing varies, although the basis for most variations is the definition of successful ageing proposed by Rowe and Kahn.¹ In this definition, the factors for successful ageing include a low probability of disease and disease-related disability, high cognitive and physical functional capacity, and active engagement in life. WHO defines healthy ageing as “the process of developing and maintaining the functional ability that enables wellbeing in older age” and acknowledges the importance of life course

influences on healthy ageing.² In WHO’s definition, healthy ageing is influenced by individual capacities and the environment, which together determine the functional ability of the individual. Globally, healthy ageing is an important societal aim because health span has not increased in parallel with the increasing life span.³ Health span is a product of multiple determinants, and it has been estimated that up to 60% of health span is modulated by social, behavioural, and environmental factors, 30% by genetic factors, and 10% by health care.⁴

The true prevalence of healthy ageing on a population level is unknown. Most studies focusing on older adults

Lancet Healthy Longev 2023; 4: e499–507

See [Comment](#) page e450

For the Finnish translation of the abstract see online for appendix 1

For the Swedish translation of the abstract see online for appendix 2

Public Health Research Program, Folkhälsan Research Center, Helsinki, Finland (T M Mikkola PhD, H Kautiainen MSc, M B von Bonsdorff PhD, N S Wasenius PhD, M K Salonen PhD, M J Haapanen DMedSc, Prof J G Eriksson DMedSc); Clinicum, Faculty of Medicine, University of Helsinki, Helsinki, Finland (T M Mikkola); Population Health Unit, Finnish Institute for Health and Welfare, Helsinki, Finland (T M Mikkola, M K Salonen, Prof E Kajantie DMedSc); Primary Health Care Unit, Kuopio University Hospital, Kuopio, Finland (H Kautiainen); Gerontology Research Center and Faculty of Sport and Health Sciences, University of Jyväskylä, Jyväskylä, Finland (M B von Bonsdorff); Department of General Practice and Primary Health Care, University of Helsinki and Helsinki University Hospital, Helsinki, Finland (N S Wasenius, M J Haapanen, Prof J G Eriksson); Department of Medical Epidemiology and Biostatistics, Karolinska Institute, Stockholm, Sweden (M J Haapanen); Clinical Medicine Research Unit, MRC Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland (Prof E Kajantie); Department of Clinical and Molecular Medicine, Norwegian University for Science and Technology, Trondheim, Norway (Prof E Kajantie); New Children’s Hospital, Helsinki University Hospital and University of Helsinki, Helsinki, Finland (Prof E Kajantie); Singapore Institute for Clinical Sciences,

Agency for Science, Technology, and Research, Brenner Centre for Molecular Medicine, Singapore (Prof J G Eriksson); Department of Obstetrics and Gynaecology and Human Potential Translational Research Programme, Yong Loo Lin School of Medicine, National University of Singapore, Singapore (Prof J G Eriksson)

Correspondence to Dr Tuja M Mikkola, Public Health Research Program, Folkhälsan Research Center, FI-00251 Helsinki, Finland tuija.mikkola@folkhalsan.fi

Research in context

Evidence before this study

Before this study, we searched previous literature in PubMed for articles published from database inception to Feb 4, 2022, using the search terms “healthy aging” or “healthy ageing”, “healthy survival”, “successful aging” or “successful ageing”, “healthy longevity”, “disease-free life expectancy”, “disease-free survival” and “healthy life expectancy”. The reference lists of identified journal articles were also searched. The literature searches were restricted to English, Finnish, and Swedish articles. Prenatal and childhood circumstances are associated with occurrence of several chronic non-communicable diseases in adulthood. From our literature search, we identified no previous studies estimating the prevalence of healthy survival, a prerequisite of healthy ageing, across adulthood. Studies on healthy ageing are often selective in terms of health and vital status because the populations typically comprise older volunteers. According to these studies, estimates of the prevalence of healthy ageing vary from 3% to 50%. However, to the best of our knowledge, no estimates of healthy survival are available in unselected population samples from a life course perspective.

Added value of this study

The present findings provide an estimate of the prevalence of healthy survival, which is an upper limit for healthy ageing. Unlike in previous studies, follow-up in the Helsinki Birth Cohort Study started from young adulthood, allowing us to account for deaths before older age. To the best of our knowledge, this is the first study to analyse associations between healthy survival and early-life and midlife factors with data collected from health records, thus avoiding recall bias. The findings indicate that at age 65 years, the probability of healthy survival was less than 50% among individuals alive in young adulthood. Early-life factors and socioeconomic status across the life course were related to healthy survival, and midlife lifestyle-related factors were associated with clinically defined healthy ageing.

Implications of all the available evidence

Promotion of healthy ageing needs to take a life course approach. A particular focus should be on social factors across the life course.

are selective in terms of health and functional status,⁵ and, perhaps more importantly, do not include individuals who have died before study sampling. These limitations introduce a bias, leading to overestimations of the proportion of individuals who age healthily. Analysis of representative national register-based data could overcome these limitations, given that register-based datasets have negligible loss of participants to follow-up.

Using a life course approach and a register-based follow-up of a unique birth cohort born in 1934–44, we quantified the probability of surviving and remaining free of chronic diseases that could affect functioning (ie, healthy survival) across adulthood. As healthy survival is a prerequisite for healthy ageing, it gives an estimate for the upper limit of the prevalence of healthy ageing in a population. Furthermore, using an extensively phenotyped subsample from the same birth cohort, we quantified the prevalence of clinically assessed healthy ageing. We also identified characteristics related to healthy survival and healthy ageing from a life course perspective.

Methods

Study design and participants

In this longitudinal study, we analysed individuals in the Helsinki Birth Cohort Study. This birth cohort comprises 13 345 individuals born at Helsinki University Central Hospital or Helsinki City Maternity Hospital in Helsinki, Finland, between 1934 and 1944, who were still alive in 1971.⁶ The cohort study excluded individuals who migrated from Finland before 1971 (n=205), resulting in a sample of 13 140 individuals (6901 men and 6239 women). Although no explicit data are available on the ethnicity of the participants, most inhabitants of Helsinki in the 1930s

and 1940s were White. The data obtained from validated national health-care registers and databases were linked to the participants with use of a unique personal identification number assigned to all Finnish residents in 1971. Childhood data (birth hospital, child welfare clinic, and school health-care records) were linked to participants using name, sex, and date of birth. The cohort was followed up from Jan 1, 1971 (mean age 30 years [SD 3], range 26–37 years) until Dec 31, 2017 (mean age 77 years [3], range 73–84 years), in total for 951 088 person-years (462 513 for women; 488 575 for men). The study was approved by the ethics committee of the Hospital District of Helsinki and Uusimaa (Helsinki, Finland; approval numbers 023/98, 344/E3/2000, and HUS/2020/2016) and the ethics committee of the National Public Health Institute (Helsinki, Finland; May 19, 1995).

Life course variables and clinical data

Early life was considered the period from fetal life to childhood up to age 12 years (maximum age represented by school health-care data) and included date of birth, birthweight, maternal BMI in late pregnancy, height at age 7 years, and childhood socioeconomic position. Midlife was defined as ranging from young to late adulthood (from age 30 years, when register data follow-up started, to age 65 years) and included years of education, income, and marital history. Date of birth, birthweight, and maternal weight and height in late pregnancy (at hospital admission for labour) were obtained from birth hospital records.⁷ In addition, data on sex were collected from the Population Register Centre. Height at age 7 years was obtained from school health-care

For the Population Register Centre see <https://dvv.fi/en/population-information-services-for-organisations>

records as previously described.⁶ Childhood socioeconomic position up to age 12 years was based on information on father's highest occupational status obtained from child welfare clinic and school health-care records. This information was extracted from the physical records of the Helsinki City Archives. The categories for childhood socioeconomic position (referring to father's occupation) were manual worker, lower-middle class, and upper-middle class according to the occupation classification by Statistics Finland.⁸ Years of education by Dec 31, 2000 were calculated on the basis of the level of the highest degree attained, obtained from Statistics Finland. The year 2000 was chosen as most participants were assumed to have attained their highest degree by that time, given that all had reached late adulthood. The level of the highest degree attained was converted to years of education according to the typical years of education (from primary school up to the highest degree attained) required for completing the degree. Household taxable gross income was obtained from Statistics Finland and mean annual income across the years 1970, 1975, and 1980 was calculated. If data were missing, income in 1985 was used. These years were chosen as being likely to reflect participant income during their working life. Household income was corrected for inflation to correspond to 2019 value in euros (the year of initial analyses) and further divided by the square root of the number of household members to obtain an estimate of income per household member.⁹ Information on marital history was obtained from the Population Register Centre, and was categorised as ever married or never married by the end of year 2017.

Clinical assessment data were based on information from clinical visits conducted in a randomly selected subsample of the Helsinki Birth Cohort (described in detail previously¹⁰) in late midlife, 2001–04 (2902 invited, 2003 clinically assessed; mean age 62 years [SD 3]) and 2017–18 (1174 invited, 815 clinically assessed; mean age 76 years [3]). The clinical assessments in 2017–18 were done as follow-up visits, meaning participants who were assessed in 2017–18 had also been assessed in 2001–04. A study flowchart and the clinical assessments of late-midlife variables are provided in appendix 3 (pp 2–3). Written informed consent was obtained from each participant in the clinical visits before any procedures were done.

Outcomes

Healthy survival was defined as being alive and without chronic diseases that are likely to have an impact on functioning. Dates of deaths were obtained from the National Death Register maintained by Statistics Finland. Dates and diagnoses (according to the International Classification of Diseases, ICD-8, ICD-9, or ICD-10) of chronic diseases were obtained from the Finnish Care Register for Health Care. The diseases included in the healthy survival variable were cancer,

stroke, other cardiovascular diseases, chronic obstructive pulmonary disease, asthma, dementia and other neurodegenerative disorders, mental disorders, neurological diseases, rheumatic diseases, osteoarthritis, dorsopathies, kidney diseases, inflammatory bowel diseases, and mental and behavioural disorders due to alcohol use (appendix 3 pp 5–6). We did not include other chronic diseases on the basis of impact on functioning. For example, hypertension and type 2 diabetes without complications were not included because these conditions, although common in older adults, do not necessarily have an impact on everyday functioning when adequately treated.

Of the 815 cohort members who took part in the clinical assessments in 2017–18, 813 had sufficient information for determining their healthy ageing status. In accordance with WHO's concept of healthy ageing and intrinsic capacity,² we defined healthy ageing as being free from major impairments in key capacities, which affect functioning in older age. Healthy ageing was defined by a range of dimensions covering: the presence of chronic diseases that could impact functioning; cognitive function; physical performance; depressive symptoms; pain interference; and social functioning (table 1). We aimed at being inclusive rather than setting high criteria for the components of healthy ageing, in accordance with our aim to yield upper estimates of the prevalence of healthy ageing. A modified Charlson Comorbidity Index (CCI)¹¹ was calculated on the basis of self-reported physician-diagnosed diseases in 2017–18. At the clinical visit, the participants were asked if they were diagnosed with any disease from a list of 26 diseases (yes or no) including 16 of 19 diseases listed in the CCI. The CCI was modified by omitting diabetes without end-organ damage, peptic ulcer disease, and mild liver disease (ie, liver disease not influencing everyday life or survival), because currently there are effective treatment modalities for these conditions. Individuals with a CCI equal to 0 and no chronic diseases from among those that were prespecified (appendix 3 pp 5–6) according to the register data met the no chronic disease criterion. The Mini-Mental State Examination¹² was administered to assess global cognitive functioning. Those with scores greater than 24 out of 30 were classified as meeting the cognitive functioning criterion.¹⁷ Physical performance was assessed with the Short Physical Performance Battery, which includes tests of balance and walking speed, and the timed chair rise test (five times).¹³ A total score greater than 8 out of 12 was the criterion for adequate physical performance.¹⁸ The participants also completed the 20-item Center for Epidemiologic Studies Depression Scale,¹⁴ and the Brief Pain Inventory¹⁵ inquiring about pain interference (7 items) on 11-point numeric rating scales. A total score lower than 20 out of 60 on the depression scale,¹⁹ and a pain interference score lower than 7 out of 10 on each interference item²⁰ were used as criteria for healthy ageing. Two items from

For the Helsinki City Archives see <https://kaupunginarkisto.helsinki.fi/en/>

For Statistics Finland's documentation on educational structure of the population see <https://www.stat.fi/en/statistics/documentation/vkour>

For the statistics on taxable incomes from Statistics Finland see <https://www.stat.fi/en/statistics/tvt>

See Online for appendix 3

For the National Death Register archive see https://www.stat.fi/tup/kuolintodistusarkisto/index_en.html

For the Finnish Care Register for Health Care see <https://thl.fi/en/web/thlfi-en/statistics-and-data/data-and-services/register-descriptions/care-register-for-health-care>

	Measure	Criterion for healthy ageing
Chronic diseases	Chronic diseases according to register-based data*; self-reported physician-diagnosed diseases as listed in the CCI (modified) ¹¹	No chronic diseases according to register-based data*; and a CCI of 0
Cognitive function	Mini-Mental State Examination ¹²	Score >24
Physical performance	Short Physical Performance Battery test ¹³	Score >8
Depressive symptoms	Center for Epidemiologic Studies Depression Scale ¹⁴	Score <20
Pain interference	Brief Pain Inventory ¹⁵	Score <7 for each pain inference item (seven items in total)
Social functioning	Medical Outcomes Study 36-item Short-Form Survey ¹⁶ ; two social functioning items on the extent and the share of time that health conditions interfere with social activities	Response on the extent item of “slightly” or less; and response on the time item of “some of the time” or less

CCI=Charlson Comorbidity Index. *Chronic diseases that were deemed likely to impact functioning and included in the healthy survival variable (appendix 3 pp 5–6).

Table 1: Dimensions and criteria for healthy ageing among cohort members who participated in clinical assessments in 2017–18

	Women		Men	
	Healthy survivors (n=1791)	Non-healthy survivors or non-survivors (n=4448)	Healthy survivors (n=1715)	Non-healthy survivors or non-survivors (n=5186)
Maternal BMI in late pregnancy, kg/m ²	26.1 (2.8)	26.2 (2.9)	26.0 (2.7)	26.3 (2.9)
Birthweight, g	3353 (467)	3333 (455)	3486 (482)	3459 (489)
Height at age 7 years, cm	119.7 (4.6)	119.9 (4.7)	120.9 (4.8)	120.6 (4.9)
Childhood socioeconomic position*				
Manual worker	981 (54.8%)	2595 (58.3%)	901 (52.5%)	3029 (58.4%)
Lower-middle class	412 (23.0%)	1068 (24.0%)	413 (24.1%)	1198 (23.1%)
Upper-middle class	344 (19.2%)	655 (14.7%)	352 (20.5%)	851 (16.4%)
Missing	54 (3.0%)	130 (2.9%)	49 (2.9%)	108 (2.1%)
Age in 1971, years	29.5 (2.6)	30.0 (2.9)	29.4 (2.5)	30.0 (2.9)
Education, years	10.1 (3.7)	10.5 (3.6)	11.4 (4.0)	10.9 (3.8)
Midlife income†, €1000	25.3 (22.3–32.1)	26.7 (20.7–34.9)	27.2 (23.0–35.3)	27.2 (21.1–34.7)
Marital status				
Ever married	1533 (85.6%)	3968 (89.2%)	1484 (86.5%)	4619 (89.1%)
Never married	258 (14.4%)	480 (10.8%)	231 (13.5%)	567 (10.9%)

Data are mean (SD), n (%), or median (IQR). *Categories refer to father's highest occupational status. †Household income divided by the square root of the number of household members.

Table 2: Early-life and midlife characteristics of the Helsinki Birth Cohort (n=13 140) stratified by healthy survival at the end of follow-up (Dec 31, 2017)

the Medical Outcomes Study 36-item Short-Form Survey¹⁶ were used to assess the extent and the share of time that physical health or emotional problems interfered with social activities. Individuals answering “slightly” or less for the extent of inference component, and “some of the time” or less on the share of time component, were classified as meeting the criteria for adequate social functioning. These cutoffs were defined on the basis of study group consensus.

Statistical analysis

We descriptively assessed early-life and midlife characteristics and compared the proportions of healthy survivors versus non-healthy survivors and non-survivors among men and women. The probability of healthy survival across adulthood in men and women was analysed with the Kaplan-Meier method with age as the timescale. The outcome event was either the occurrence of a chronic disease or death, and individuals who emigrated from Finland were censored on the date of emigration (n=835 by end of follow-up). The probability of being healthy (ie, free of chronic disease) among individuals who were alive was analysed with Cox regression models, with death and emigration as censoring events (n=1866 by end of follow-up). In survival models, follow-up started on Jan 1, 1971, and ended on Dec 31, 2017. Univariable and multivariable Cox regression models were used to analyse the associations of early-life and midlife characteristics with healthy survival (inverse hazard ratio [HR] and 95% CIs) stratified by sex. Multivariable Cox regression models were adjusted for potential confounders: analyses of maternal BMI in late pregnancy and childhood socioeconomic position were adjusted for birth year; analysis of birthweight was adjusted for birth year and maternal BMI in late pregnancy; analysis of height at age 7 years was adjusted for birth year, maternal BMI in late pregnancy, birthweight, and childhood socioeconomic position; analysis of years in education was adjusted for birth year, height at age 7 years, and childhood socioeconomic position; and analysis of marital status was adjusted for birth year, height at age 7 years, childhood socioeconomic position, and years in education. We chose to include only one indicator of socioeconomic position in midlife in the models; given that education is typically a determinant of income, we included years of education rather than income. The proportional hazards assumption was confirmed for all variables with Schoenfeld's tests and by visual inspection of graphed Schoenfeld residuals and log-log plots. Among individuals who completed clinical assessments in 2001–04 and 2017–18, the associations between healthy ageing status in 2017–18 and late-midlife variables assessed in 2001–04 were analysed with univariable and age-adjusted logistic regression models to obtain odds ratios (ORs) and 95% CIs, with healthy ageing as the outcome variable. All data were analysed via an available-case analysis method with pairwise deletion.

The level of significance was set at 0.05 and was interpreted from 95% CIs. The widths of 95% CIs were not adjusted for multiplicity and thus the intervals cannot be used in place of hypothesis testing. The data were analysed in Stata (version 17.0).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Of the 13 140 individuals in the Helsinki Birth Cohort Study, 3506 (26.7%) were healthy survivors at the end of follow-up on Dec 31, 2017. In both sexes, healthy survivors were born to mothers with lower BMI, and healthy survivors appeared to have higher birthweight, higher childhood socioeconomic position, and younger age at the start of follow-up (Jan 1, 1971) than non-healthy survivors or non-survivors, although differences were small (table 2). In addition, a slightly smaller proportion of healthy survivors had been married versus non-healthy survivors or non-survivors.

We assessed the probability of healthy survival during adulthood (figure, part A). Women had a lower probability of healthy survival than men between ages 39 and 65 years, with no overlap of 95% CIs in this range (data not shown). At age 65 years, the probability of healthy survival was 42.8% (95% CI 41.6–44.0) in men and 40.1% (38.9–41.4) in women. At age 75 years, the probability of healthy survival was slightly lower in men than in women (men 22.5% [21.5–23.6]; women 24.4% [23.3–25.6]) although 95% CIs overlapped. The crude HR for healthy survival was 0.97 (95% CI 0.93–1.01) in men compared with women at age 75 years.

We also assessed the probability of being healthy (free of chronic diseases) during adulthood among individuals who were alive (figure, part B). The probability of being healthy at age 65 years was 47.8% (95% CI 46.5–49.0) in men and 41.9% (40.6–43.5) in women. At age 75 years, the probabilities were 27.5% (26.3–28.6) in men and 27.1% (25.9–28.3) in women.

In the crude survival models, higher childhood socioeconomic position, a longer time in education, and ever being married were associated with an increased likelihood of healthy survival among women (table 3). After multivariable adjustment, the association of childhood socioeconomic position and time in education persisted. In addition, shorter height at age 7 years became significantly associated with healthy survival. Among men, lower maternal BMI in late pregnancy, higher birthweight, taller height at age 7 years, higher childhood socioeconomic position, a longer time in education, and ever being married were associated with an increased likelihood of healthy survival in the crude survival models. After adjustment for potential confounders, the association of maternal BMI persisted, the association of time in education weakened but persisted, and the association of childhood socioeconomic position was strengthened. (table 3).

Among the 813 individuals who participated in the clinical assessments in 2017–18 (mean age 76 years [SD 3]) and provided sufficient data to determine healthy ageing status, 159 (19.6%) were healthy agers, meeting all six criteria of healthy ageing (table 1). 381 (46.9%) participants met five criteria, 169 (20.8%) met four criteria, and 104 (12.8%) met three or fewer criteria.

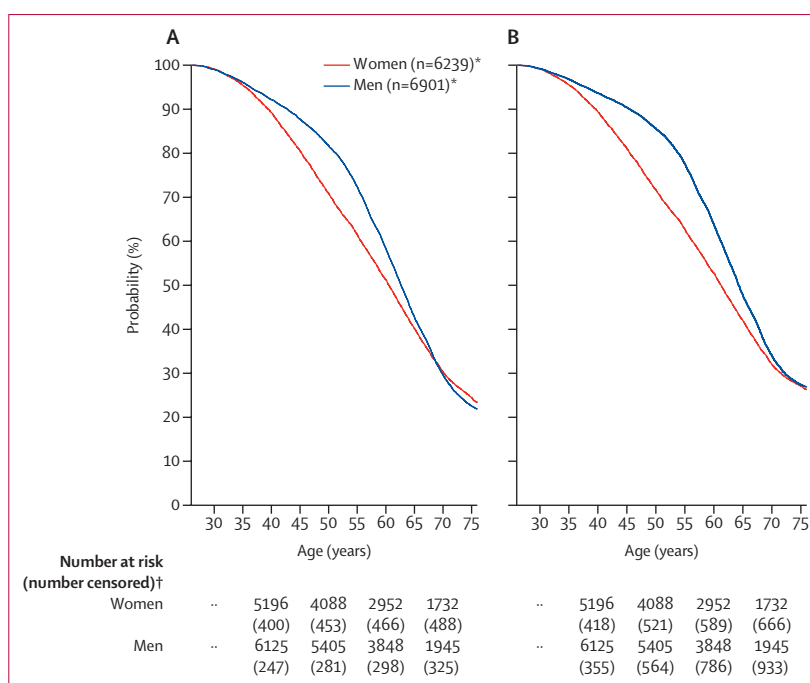


Figure: Probability of healthy survival and of being healthy in the Helsinki Birth Cohort (n=13 140) (A) Probability of healthy survival (ie, alive and free of chronic disease) as a function of age in women and men up to age 75 years. (B) Probability of being healthy (ie, free of chronic disease) as a function of age among women and men who were alive. *Total men and women at risk in the Helsinki Birth Cohort Study. †Cumulative number censored; censoring events were emigration in the analysis in part A and emigration and death in the analysis in part B.

	Women		Men	
	HR (95% CI)	Adjusted HR (95% CI)	HR (95% CI)	Adjusted HR (95% CI)
Birth year, per year	1.00 (0.99–1.01)	NA	1.00 (0.99–1.01)	NA
Maternal BMI in late pregnancy, per 1 SD increase	0.98 (0.95–1.02)	0.98 (0.95–1.02)*	0.93 (0.91–0.96)	0.93 (0.90–0.96)*
Birthweight, per 1 SD increase	1.01 (0.98–1.04)	1.00 (0.97–1.03)†	1.03 (1.00–1.05)	1.03 (0.99–1.06)†
Height at age 7 years, per 1 SD increase	0.97 (0.93–1.01)	0.95 (0.91–0.99)‡	1.05 (1.01–1.09)	0.99 (0.95–1.03)‡
Childhood SEP				
Manual worker	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Lower-middle class	1.00 (0.93–1.08)	1.01 (0.94–1.09)*	1.06 (1.00–1.14)	1.11 (1.04–1.20)*
Upper-middle class	1.15 (1.05–1.25)	1.15 (1.05–1.26)*	1.11 (1.02–1.20)	1.21 (1.11–1.31)*
Education years, per 1 SD increase	1.04 (1.01–1.06)	1.03 (1.00–1.07)§	1.19 (1.15–1.22)	1.12 (1.08–1.16)§
Ever married, yes vs no	1.15 (1.05–1.27)	1.08 (0.96–1.22)¶	1.32 (1.22–1.45)	1.11 (0.99–1.25)¶

If the confidence interval of the HR does not cross 1, the p value is <0.05 and statistically significant. Standard deviations were for men and women separately. Categories for childhood SEP refer to father's highest occupational status. HR=hazard ratio. NA=not applicable. SEP=socioeconomic position. *Adjusted for birth year. †Adjusted for birth year and maternal BMI in late pregnancy. ‡Adjusted for birth year, maternal BMI in late pregnancy, birthweight, and childhood SEP. §Adjusted for birth year, height at age 7 years, and childhood SEP. ¶Adjusted for birth year, height at age 7 years, childhood SEP, and years in education.

Table 3: HRs for the association between early-life and midlife factors and healthy survival in the Helsinki Birth Cohort Study (n= 13 140) stratified by sex

	Healthy ageing (n=159)	Non-healthy ageing (n=654)	Crude OR* (95% CI) for healthy ageing	Age-adjusted OR* (95% CI) for healthy ageing
Sex				
Men	67 (42.1%)	289 (44.2%)	1 (ref)	1 (ref)
Women (vs men)	92 (57.9%)	365 (55.8%)	1.08 (0.77–1.54)	1.11 (0.78–1.58)
Age, years	60 (2)	61 (3)	0.88 (0.81–0.94)	NA
BMI, kg/m ²	26.8 (3.5)	27.2 (4.2)	0.99 (0.95–1.03)	0.99 (0.95–1.03)
Body fat percentage, %				
Men	22.3 (5.3)	22.6 (5.6)	0.98 (0.94–1.01)	0.98 (0.95–1.02)
Women	32.4 (6.2)	33.2 (6.5)	0.99 (0.97–1.02)	0.99 (0.97–1.02)
Waist circumference, cm				
Men	98.3 (9.0)	99.4 (11.0)	0.99 (0.96–1.02)	0.99 (0.96–1.01)
Women	88.2 (10.6)	89.5 (11.6)	0.99 (0.97–1.01)	0.99 (0.98–1.01)
Grip strength, kg				
Men	40.1 (8.8)	41.0 (9.9)	0.99 (0.96–1.02)	1.00 (0.98–1.02)
Women	24.3 (5.4)	23.0 (6.7)	1.03 (0.99–1.07)	1.03 (1.01–1.06)
Systolic blood pressure, mm Hg	143 (21)	143 (19)	1.00 (0.99–1.01)	1.00 (0.99–1.01)
Diastolic blood pressure, mm Hg	89 (11)	88 (10)	1.01 (0.99–1.03)	1.00 (0.99–1.01)
Fasting plasma glucose, mmol/L	5.59 (0.84)	5.63 (0.96)	0.96 (0.79–1.16)	0.93 (0.78–1.12)
LDL cholesterol, mmol/L	3.67 (0.86)	3.64 (0.88)	1.04 (0.85–1.27)	1.23 (1.03–1.47)
HDL cholesterol, mmol/L	1.65 (0.47)	1.63 (0.42)	1.07 (0.55–2.08)	1.08 (0.69–1.70)
Triglycerides, mmol/L	1.45 (0.78)	1.43 (0.76)	1.03 (0.82–1.28)	0.97 (0.74–1.28)
C-reactive protein, mg/L	2.41 (3.19)	3.28 (6.03)	0.96 (0.92–1.02)	1.00 (0.96–1.03)
Married or co-habiting (vs not married or co-habiting)	126 (79.2%)	514 (78.6%)	1.04 (0.68–1.59)	1.04 (0.71–1.52)
Income, €1000	13.2 (9.8–18.9)	10.9 (7.7–16.1)	1.01 (1.00–1.03)	1.00 (0.99–1.01)
Smoking history (vs non-smoker)				
Former smoker	46 (28.9%)	247 (37.8%)	0.65 (0.44–0.96)	0.68 (0.47–0.98)
Current smoker	25 (15.7%)	107 (16.4%)	0.81 (0.49–1.34)	0.76 (0.37–1.53)
Alcohol consumption at least once a week (vs less than once a week)	86 (54.1%)	364 (55.7%)	0.95 (0.67–1.35)	1.07 (0.75–1.52)
Physical activity, metabolic equivalent hours of task per week	36.6 (21.7)	38.2 (25.9)	1.00 (0.99–1.01)	1.01 (0.99–1.02)
Alternative Healthy Eating Index	65.8 (8.4)	63.6 (9.1)	1.03 (1.01–1.05)	1.03 (1.01–1.05)
Diabetes medication (vs non-user)	6 (3.8%)	36 (5.5%)	0.67 (0.28–1.63)	0.88 (0.54–1.43)
Lipid-lowering medication (vs non-user)	18 (11.3%)	109 (16.7%)	0.64 (0.37–1.09)	0.60 (0.42–0.87)
Antihypertensive medication (vs non-user)	36 (22.6%)	201 (30.7%)	0.66 (0.44–0.99)	0.90 (0.63–1.29)
Relative telomere length, T/S ratio	1.39 (0.29)	1.40 (0.33)	0.87 (0.50–1.53)	0.82 (0.46–1.47)

Data are mean (SD), n (%), or median (IQR). If the confidence interval of the OR does not cross 1, the p value is <0.05 and statistically significant. Assessments of variables are described in appendix 3 (pp 2–3). OR=odds ratio. NA=not applicable. T/S=ratio of telomere DNA to haemoglobin subunit beta single-copy gene signal intensities. *OR values are per 1 unit increase for quantitative variables; for qualitative variables, reference categories are given in parentheses in the left column.

Table 4: Characteristics of participants (n=813) at the clinical assessment in 2001–04 according to healthy ageing status in 2017–18 and crude and age-adjusted ORs for healthy ageing

Analysis of the associations of late-midlife variables measured in 2001–04 (mean age 61 years [SD 3]) with healthy ageing status in 2017–18 showed age was an important determinant of healthy ageing in univariable analysis (crude OR 0.88 [95% CI 0.81–0.94]; table 4). Three factors were associated with increased odds of healthy ageing in the age-adjusted analyses: greater hand grip strength in women, higher LDL cholesterol concentration, and healthier eating habits (higher Alternative Healthy Eating Index²¹) in all participants. Former smoking and use of lipid-lowering medication were associated with reduced odds of healthy ageing.

Discussion

By applying a life course approach and using validated register-based data, we showed that from age 65 years, the probability of healthy survival was less than 50% among members of the original Helsinki Birth Cohort Study. In addition, only around a fifth of individuals who participated in a clinical assessment at mean age 76 years met all clinical criteria for healthy ageing. Early-life factors including childhood socioeconomic status, and years in education by adulthood, were related to healthy survival.

A strength of the present study is the long-term follow-up of the cohort from birth to older age. The register-based follow-up also gives a comprehensive picture of morbidity and mortality across adulthood and minimises loss to follow-up. High completeness and validity of the Finnish Care Register for Health Care have been reported.²² However, healthy survival is a broad concept, and the register-based data allowed only a limited operationalisation of healthy survival. In 1934–44, about 46 000 livebirths were reported in Helsinki, and the birth cohort in this study was restricted to individuals who had attended child welfare clinics, which were voluntary. Thus, the register-based sample might have been biased in terms of socioeconomic status. However, the distribution of paternal occupational status in the Helsinki Birth Cohort Study is consistent with the occupational distribution in Helsinki 80 years ago among families.²³ The sample also excluded people who had died before 1971, so that only individuals with a national personal identification number (assigned to all residents of Finland in 1971) were included, allowing for register data linkage. Subsamples of the cohort have also been extensively phenotyped from late midlife to older age. Thus, the cohort forms a unique data source to study healthy ageing from a life course perspective. There was loss to follow-up in the clinical part of the study, which is typical of samples of older populations and to some extent unavoidable. This loss in the clinical sample is likely to be dependent on health status (ie, those with poorer health were less likely to participate) as the participants were required to travel to the laboratory, thus potentially introducing bias to the analysis of healthy ageing. The model of healthy survival allowed only

transitions from healthy status to non-healthy status, and not the reverse transition. However, it is possible that some individuals might have transitioned from non-healthy to healthy status. Therefore, the model might have slightly underestimated the proportion of healthy survival. Our definition of healthy ageing was similar to the concept of intrinsic capacity in the definition of healthy ageing by WHO² although it partly differs from the widespread operationalisation of intrinsic capacity by Cesari and colleagues.²⁴ In WHO's definition, intrinsic capacity and environment together determine healthy ageing. Although environmental influence was not considered in our definition, healthy ageing concepts with similar elements to those included in the present study have been used in the research literature.^{25,26} Of note, the members of the Helsinki Birth Cohort experienced World War 2 during different phases of their childhood, which might have had an impact on their health. War strains in Helsinki were diverse and changing and included, among others, air raids, food shortages, and the threat of occupation and, for some of the children, evacuation abroad without their parents.

As healthy survival is a prerequisite for healthy ageing, the present findings on the probability of healthy survival suggest that the upper limit for healthy ageing is less than 50% at age 65 years, and less than 25% at age 75 years. In previous studies, the prevalence of healthy ageing has ranged from 3% to 50%.²⁵⁻²⁷ However, most previous studies on healthy ageing did not have a follow-up from birth and thus individuals were inherently selected according to vital and health status. Our study minimised selection bias by analysing national register-based data in a population-based cohort with little loss to follow-up from young adulthood to older age.

Healthy survival was lower among women than men up to age 65 years. It is well established that morbidity is higher among women although they live longer than men.²⁸ Accordingly, the present study showed that less women than men were healthy (free of chronic diseases) among those alive. Women have more non-fatal chronic conditions that cause disability, such as arthritis, but men are more likely to have life-threatening events, such as cardiovascular diseases and fatal accidents.²⁹ These differences are likely to be explained by biological factors, such as differing immune response, and social and behavioural factors, such as smoking.²⁹ We also cannot exclude the possibility that sex differences in help-seeking behaviours contribute to the findings.

The likelihood of being healthy among individuals alive at defined ages provides an important frame of reference for cross-sectional studies estimating the true prevalence of healthy ageing in cohorts of older adults. For cohort members who were alive, the probability of being free of chronic diseases was less than 50% at age 65 years, and less than 30% at age 75 years. Thus, healthy ageing seems to be possible only in a minority of older adults. When considering our clinical sample, although

likely to be healthier than the general Finnish population of the same age, only 20% were healthy agers at the mean age of 76 years, according to clinical criteria covering several dimensions of health and functioning. This estimate is in accordance with the healthy ageing estimate at mean age 74 years from The Singapore Chinese Health Study, which applied a similar definition of healthy ageing.²⁶

Our findings further suggest that early-life factors are associated with healthy survival, corresponding with the Developmental Origins of Health and Disease theory, according to which the prenatal period and early childhood period are crucial for the development of health.^{30,31} In the present study, increased maternal BMI in pregnancy was associated with a lower probability of healthy survival in men. This association was not apparent in women. Taller height at age 7 years was associated with reduced probability of healthy survival in women in the adjusted model. Some sex differences in associations between early growth and morbidity in adulthood have previously been observed, but findings have not been consistent across studies.³² The low strength of associations we observed between early-life factors and healthy survival was expected, considering the long time between the exposures and outcome. Existing evidence on the associations between prenatal and childhood circumstances and various chronic non-communicable diseases are mostly from follow-up studies until middle age.^{6,7,33} The present findings suggest that the effect of early life circumstances on health extends beyond midlife until the end of the lifespan.

Socioeconomic factors are associated with a wide spectrum of health outcomes across the life course.^{34,35} In the present study, a longer time in education increased the likelihood of healthy survival, particularly in men. We also found evidence of an association between higher childhood socioeconomic status and healthy survival in both sexes. Education might have been a stronger determinant of occupational status and wealth for men than for women, as at the time, the socioeconomic status of women might have depended more on their husband's education, and therefore income and occupational status, than their own. The influence of childhood socioeconomic status on mortality has been shown to persist until old age.³⁴ However, the present study is, to the best of our knowledge, the first to report a relationship between an objective indicator of childhood socioeconomic status and healthy ageing.

Only a few factors at around age 60 years were associated with clinically defined healthy ageing in later life. The healthy agers, besides being slightly younger, were less likely to have a smoking history, less likely to be using lipid-lowering medication, and had healthier eating habits than the non-healthy agers at around age 60 years. The Alternative Healthy Eating Index used in the present study has been shown to be associated with healthy ageing²⁶ and to be predictive of the risk of several

For the Helsinki Statistical Yearbooks see https://www.helsinki.fi/static/tieke/digitoidut_asiakirjat/helsingin_kaupungin_tilastolliset_vuosikirjat/index.html

chronic diseases, such as cardiovascular diseases and cancer.²¹ Although systemic biomarkers were not associated with healthy ageing, it is possible that at the cellular level there are common denominators for age-related diseases and functional decline.³⁶

The present study supports the life course approach to healthy ageing, highlighting the importance of early life factors, and of socioeconomic factors throughout the life course. By applying this understanding, a focus on preventive efforts among individuals who are less advantaged in terms of socioeconomic position could prove beneficial. The life course approach emphasises that the health and circumstances in one phase of life are not isolated events, but largely influence health and wellbeing in later life stages. Therefore, strategies that enhance individual capacities and potential during growth, young adulthood, and midlife have the potential to promote healthy ageing for as long as possible.

Contributors

TMM, HK, MBvB, NSW, and JGE conceptualised the study. HK and MKS curated data. TMM and HK did the formal analysis. JGE acquired funding. MBvB, MJH, MKS, EK, and JGE led the investigation. JGE designed the methodology. MKS and JGE were project administrators. JGE supervised the study. HK was responsible for data visualisation. TMM wrote the original draft. HK, MBvB, NSW, MKS, MJH, EK, and JGE reviewed and edited the manuscript. TMM and HK directly accessed and verified the underlying data reported in the manuscript. All authors had full access to all the data in the study and had final responsibility to submit for publication.

Declaration of interests

TMM has received research grants from Medicinska Understödsföreningen Liv och Hälsa. MBvB has received research grants from the Academy of Finland. MJH has received research grants from Finska Läkaresällskapet and Medicinska Understödsföreningen Liv och Hälsa. EK has received funding from the Academy of Finland, the Finnish Pediatric Research Foundation, Sigrid Jusélius Foundation, the Signe and Ane Gyllenberg Foundation, the Finnish Foundation for Cardiovascular Research, the Finnish Diabetes Research Foundation, Finska Läkaresällskapet, Novo Nordisk Foundation, and the Yrjö Jahnsson Foundation. JGE has received funding for the submitted work from the Signe and Ane Gyllenberg Foundation, Samfundet Folkhälsan, Finska Läkaresällskapet, Medicinska Understödsföreningen Liv och Hälsa, the European Commission within the Seventh Framework Programme, the EU Horizon 2020 programme, and the Academy of Finland. All other authors declare no competing interests.

Data sharing

The data obtained from national registers, databases, and health records that support the findings of this study are available from the Finnish Institute for Health and Welfare, although restrictions apply to the availability of these data, which were used under licence for the current study and so are not publicly available. All data are available from the authors (tuija.mikkola@folkhalsan.fi) upon reasonable request, and after the authors have applied for permission to share the data from the Finnish Institute for Health and Welfare. For the register data, additional licences are needed from the Finnish Institute for Health and Welfare.

Acknowledgments

This work was supported by the Signe and Ane Gyllenberg Foundation, Samfundet Folkhälsan, Finska Läkaresällskapet, Medicinska Understödsföreningen Liv och Hälsa, the European Commission within the Seventh Framework Programme (project DORIAN, grant agreement number 278603), and the EU Horizon 2020 programme (project LifeCycle, grant number 733206; and project DYNAHEALTH, grant number 633595). The Academy of Finland supported JGE (grant numbers 129369, 129907, 135072, 129255, and 126775).

References

- Rowe JW, Kahn RL. Successful aging. *Gerontologist* 1997; 37: 433–40.
- WHO. World report on ageing and health. 2015. <https://apps.who.int/iris/handle/10665/186463> (accessed April 10, 2023).
- Salomon JA, Wang H, Freeman MK, et al. Healthy life expectancy for 187 countries, 1990–2010: a systematic analysis for the Global Burden Disease Study 2010. *Lancet* 2012; 380: 2144–62.
- Schroeder SA. Shattuck Lecture. We can do better—improving the health of the American people. *N Engl J Med* 2007; 357: 1221–28.
- Chatfield MD, Brayne CE, Matthews FE. A systematic literature review of attrition between waves in longitudinal studies in the elderly shows a consistent pattern of dropout between differing studies. *J Clin Epidemiol* 2005; 58: 13–19.
- Osmond C, Kajantie E, Forsén TJ, Eriksson JG, Barker DJP. Infant growth and stroke in adult life: the Helsinki birth cohort study. *Stroke* 2007; 38: 264–70.
- Forsén T, Eriksson JG, Tuomilehto J, Teramo K, Osmond C, Barker DJ. Mother's weight in pregnancy and coronary heart disease in a cohort of Finnish men: follow up study. *BMJ* 1997; 315: 837–40.
- Statistics Finland. Classification of socioeconomic groups: handbooks, 17. Helsinki: Statistics Finland, 1989.
- Atkinson AB, Smeeding TM. Income distribution in OECD countries. Evidence from the Luxembourg Income Study. Paris: Organisation for Economic Co-operation and Development, 1995.
- Ylihärsilä H, Kajantie E, Osmond C, Forsén T, Barker DJP, Eriksson JG. Body mass index during childhood and adult body composition in men and women aged 56–70 y. *Am J Clin Nutr* 2008; 87: 1769–75.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40: 373–83.
- Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; 12: 189–98.
- Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol* 1994; 49: M85–94.
- Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas* 1977; 1: 385–401.
- Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singap* 1994; 23: 129–38.
- Ware JE, Snow KK, Kosinski M, Gandek B. SF-36 health survey: manual and interpretation guide. Boston, MA: Health Institute, New England Medical Center, 1993.
- Creavin ST, Wisniewski S, Noel-Storr AH, et al. Mini-Mental State Examination (MMSE) for the detection of dementia in clinically unevaluated people aged 65 and over in community and primary care populations. *Cochrane Database Syst Rev* 2016; 4: CD011145.
- Bergland A, Strand BH. Norwegian reference values for the Short Physical Performance Battery (SPPB): the Tromsø Study. *BMC Geriatr* 2019; 19: 216.
- Beekman AT, Deeg DJH, Van Limbeek J, Braam AW, De Vries MZ, Van Tilburg W. Criterion validity of the Center for Epidemiologic Studies Depression scale (CES-D): results from a community-based sample of older subjects in the Netherlands. *Psychol Med* 1997; 27: 231–35.
- Serlin RC, Mendoza TR, Nakamura Y, Edwards KR, Cleeland CS. When is cancer pain mild, moderate or severe? Grading pain severity by its interference with function. *Pain* 1995; 61: 277–84.
- Chiuvè SE, Fung TT, Rimm EB, et al. Alternative dietary indices both strongly predict risk of chronic disease. *J Nutr* 2012; 142: 1009–18.
- Sund R. Quality of the Finnish Hospital Discharge Register: a systematic review. *Scand J Public Health* 2012; 40: 505–15.
- Siipi J. Pääkaupunkiyhteiskunta ja sen sosiaalipolitiikka. In: Rosen R, Hornborg E, Jutikkala E, Waris H, Castren M, eds. Helsingin kaupungin historia. 5.osa, 1. nide, ajanjakso 1918–1945. Helsinki: Helsingin kaupunki, 1962: 137.
- Cesari M, Araujo de Carvalho I, Amuthavalli Thiyagarajan J, et al. Evidence for the domains supporting the construct of intrinsic capacity. *J Gerontol A Biol Sci Med Sci* 2018; 73: 1653–60.

- 25 Jaspers L, Schoufour JD, Erler NS, et al. Development of a Healthy Aging Score in the population-based Rotterdam Study: evaluating age and sex differences. *J Am Med Dir Assoc* 2017; **18**: 276.e1–7.
- 26 Zhou YF, Song XY, Wu J, et al. Association between dietary patterns in midlife and healthy ageing in Chinese adults: the Singapore Chinese Health Study. *J Am Med Dir Assoc* 2021; **22**: 1279–86.
- 27 McLaughlin SJ, Jette AM, Connell CM. An examination of healthy aging across a conceptual continuum: prevalence estimates, demographic patterns, and validity. *J Gerontol A Biol Sci Med Sci* 2012; **67**: 783–89.
- 28 Wingard DL. The sex differential in morbidity, mortality, and lifestyle. *Annu Rev Public Health* 1984; **5**: 433–58.
- 29 Oksuzyan A, Juel K, Vaupel JW, Christensen K. Men: good health and high mortality. Sex differences in health and aging. *Aging Clin Exp Res* 2008; **20**: 91–102.
- 30 Barker DJP. The developmental origins of chronic adult disease. *Acta Paediatr Suppl* 2004; **93**: 26–33.
- 31 Fleming TP, Watkins AJ, Velazquez MA, et al. Origins of lifetime health around the time of conception: causes and consequences. *Lancet* 2018; **391**: 1842–52.
- 32 Intapad S, Ojeda NB, Dasinger JH, Alexander BT. Sex differences in the developmental origins of cardiovascular disease. *Physiology (Bethesda)* 2014; **29**: 122–32.
- 33 Barker DJP, Winter PD, Osmond C, Margetts B, Simmonds SJ. Weight in infancy and death from ischaemic heart disease. *Lancet* 1989; **2**: 577–80.
- 34 Ericsson M, Pedersen NL, Johansson ALV, Fors S, Dahl Aslan AK. Life-course socioeconomic differences and social mobility in preventable and non-preventable mortality: a study of Swedish twins. *Int J Epidemiol* 2019; **48**: 1701–09.
- 35 Stringhini S, Carmeli C, Jokela M, et al. Socioeconomic status and the 25 × 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1·7 million men and women. *Lancet* 2017; **389**: 1229–37.
- 36 Kennedy BK, Berger SL, Brunet A, et al. Geroscience: linking aging to chronic disease. *Cell* 2014; **159**: 709–13.